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Reply

We want to thank Dr Kok for his interest in our work and insightful comments. As Dr Kok points out, the literature with respect to the potential clinical benefits of statin drugs is rapidly growing, and it is clear that the efficacy of these agents extends well beyond cholesterol-lowering and protection from coronary events. Multiple medical trials have now demonstrated a significant reduction in long-term stroke incidence among patients with elevated cholesterol levels, but nonstatin cholesterol-lowering therapies have not resulted in such a reduction in stroke morbidity in this patient population.

What is particularly intriguing is the observation that among patients with normal cholesterol levels, statins have been associated with a significant reduction in long-term stroke incidence.[1] We believe this strongly suggests that the lipid-independent pleiotropic activities of statins are likely responsible for these clinical observations. It is within this context that we sought to investigate whether statin drug use might convey a protective effect in the acute setting among patients undergoing carotid endarterectomy (CEA), a highly effective stroke-preventing operation.

The pleiotropic effects of statins extend beyond plaque stabilization and include improvements in endothelial function through a nitric-oxide dependent process, as well as anti-inflammatory, antithrombotic, and antioxidant activities. The incidence of perioperative stroke is lower among patients undergoing CEA for asymptomatic vs symptomatic disease, but asymptomatic patients still do experience perioperative strokes. In fact, there is growing evidence that a percentage of patients with asymptomatic carotid disease have experienced so-called silent strokes, as evident by computed tomography or magnetic resonance imaging studies.[2] And clearly, some patients with asymptomatic carotid stenoses may have more unstable plaques than others. So, it is absolutely logical and appropriate to include asymptomatic patients in our analysis.

We are well aware of the publication by Kennedy et al[3] that appeared in the literature several months after our data were initially presented at the annual meeting of the Society for Vascular Surgery. Their study differs from ours in that the beneficial effects of statin therapy were only demonstrated among symptomatic patients. Although plaque stabilization is an attractive hypothetical explanation for the clinical benefit of statins among patients undergoing CEA and may even reduce morbidity among clinically asymptomatic patients with plaques at risk, the other pleiotropic actions of statins may also be operative to some degree in both asymptomatic and symptomatic patients. Moreover, it appears that the majority of CEAs in contemporary practice are now performed in asymptomatic patients. By including asymptomatic patients in our study, we believe our analysis is more rigorous and our conclusions more generalizeable to the entire population of patients with carotid stenosis than the Kennedy et al study.

The nature of our retrospective analysis, unfortunately, did not allow us to determine with certainty the specific cause of mortality in this decade-long experience. Although it is established in nonsurgical patients that statins reduce cardiac mortality, our cohorts were heterogeneous, with statin-users having considerably more cardiovascular risk factors. Nevertheless, the incidence of 30-day myocardial infarction in statin users was lower (1.2% vs 2.1%), based on a total of 27 clinical events detailed in Table II. The relatively small number of cardiac events in this study precluded this trend from having the power to achieve statistical significance. And it is worth noting that the analysis of symptomatic patients by Kennedy et al[3] similarly found no statistically significant difference in the frequency of cardiac outcomes between statin users and nonstatin users. But as Dr Kok surely knows, we must be careful in our analysis of clinical outcome studies to distinguish the difference between clinical and statistical significance.

With respect to the validity of our multivariate analysis, the variable contralateral stenosis was indeed tested in this model but did not reach statistical significance. Variables that trended towards significance in univariate analysis were included in multivariate analysis as described; however, any variable that did not achieve significance in both the multivariate and univariate analysis was removed from the final multivariate model. Contralateral stenosis did not reach significance in univariate ($P = .081$) or multivariate analysis ($P = .32$), thus it was taken out of the final model. Furthermore, including contralateral stenosis in the multivariate model does not change the four independent predictors of mortality, which were carotid endarterectomy/coronary artery bypass grafting, chronic renal insufficiency, atrial fibrillation, and statin use. Thus, the impact of this variable does not affect the statistical significance of statin use on mortality, and our conclusions remain the same.

Our group is obviously excited about the novel findings of this study and the implications for our patients. We believe that statin use may represent a useful and logical strategy for making a very effective and safe operation even better.

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Regarding "Evidence for early nasogastric tube removal after infrarenal aortic surgery: A randomized trial"

In view of the lack of objective data regarding nasogastric decompression in aortic surgery, Goueffic's group (J Vasc Surg 2005;42:654-9) have provided some useful information regarding the practice. However, we feel that their data must be interpreted with some care.

By their own admission, their series lacks sufficient power to reliably establish equivalence between early and late withdrawal of nasogastric decompression. They did demonstrate an increased rate of respiratory complications, primarily pneumonia, in the late removal group. Unfortunately, they provide no data regarding the postoperative fluid management of their patients. To date, two trials[1,2] have reported the results of postoperative fluid restriction vs "standard" fluid management with 1 liter of 0.9% saline and 2 liters of 5% dextrose per day in colorectal surgical patients. Lobo[2] demonstrated a reduction in ileus, reduced length of stay, and reduced risk of other complications. Brandstrup[1] also reported a lower risk of complications amongst the restricted arm of his trial, including cardiopulmonary complications.